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Award Number:
W81XWH-08-2-0104

TITLE:
CBT for Nightmares in OEF/OIF Veterans

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REPORT DATE:
July 2009

TYPE OF REPORT:
Annual Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED *(From - To)*
01-07-2009	Annual	1 July 2008–30 June, 2009

4. TITLE AND SUBTITLE
CBT for Nightmares in OEF/OIF Veterans

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-08-2-0104

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Philadelphia Research and Education Foundation
Philadelphia, PA 19104

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research
And Materiel Command
Fort Detrick, Maryland
21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This study examines the efficacy of two cognitive-behavioral treatments for PTSD-related recurrent nightmares and other sleep difficulties in veterans of Operations Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) in a randomized controlled trial. Participants will be 160 OEF/OIF veterans presently in outpatient treatment for PTSD at one of two study sites, the Philadelphia VAMC or the VACHS, West Haven, CT.

During Year One of this award, the study procedures have received approval by four regulatory bodies (PVAMC IRB, VACHS IRB, Yale University IRB and DoD HRPO). Further, the study was launched at the Philadelphia site and enrollment is under way. Data will be analyzed at the end of the data collection period and therefore research findings are not yet available.

15. SUBJECT TERMS
Posttraumatic Stress Disorder, Nightmares, Randomized Controlled Trial, Cognitive-behavioral Treatment, OEF/OIF Veterans

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	8	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

Section I: Introduction

A substantial proportion of veterans returning from Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) have significant psychological symptoms related to traumatic war zone exposure, including recurrent nightmares and other sleep disturbances. Nightmares are generally distressing and difficult to treat, often persisting despite successful resolution of other Posttraumatic Stress Disorder (PTSD) symptoms. A cognitive-behavioral treatment (CBT), Imagery Rehearsal (IR), appears to have promise for successfully treating nightmares. This study investigates the efficacy of IR in treating OEF/OIF veterans, many of whom likely have mild to moderate traumatic brain injury (TBI). There are three main objectives of this study: 1) to examine the efficacy of IR, combined with psychoeducation about PTSD and nightmares and standard CBT for insomnia (IR + PPCI), compared to psychoeducation about PTSD and nightmares and CBT for insomnia (PPCI) alone, in reducing nightmare frequency and improving global sleep quality in OEF/OIF veterans with PTSD; 2) to determine whether there are moderating effects of neurocognitive impairment on the efficacy of these two forms of CBT for nightmares; and 3) to explore possible neurobiological correlates of treatment-related changes in nightmare frequency and sleep quality, focusing on noradrenergic systems. One hundred and sixty OEF/OIF veterans enrolled in treatment for PTSD at the Philadelphia VA Medical Center (PVAMC) or the VA Connecticut Health Care System (VACHS), West Haven Campus, will be randomized to one of two individual treatments: IR + PPCI or PPCI alone. Participants are referred by their mental health treatment providers and assessed for PTSD and war zone-related nightmares. Participants complete a battery of computerized neuropsychological tests at baseline and are stratified in their randomization to either group depending on the results. Once randomized, participants meet for 6 weekly individual sessions of IR + PPCI or PPCI alone. Participants complete self-report questionnaires assessing nightmares, sleep quality, PTSD, and depression, at baseline, immediately after treatment, and again three and six months after treatment. Additionally, participants provide saliva samples for measurement of salivary alpha-amylase, a marker of peripheral noradrenergic activity, both before sleep onset and upon awakening, for two nights before treatment and for two nights before the first post-treatment assessment.

Section II: Progress to Date on 5 Study Tasks in Approved Statement of Work:

1. Obtaining approvals for the study protocol at the study locations.

A. Philadelphia VAMC/University of Pennsylvania:

- Regulatory review of the initial protocol was completed by the PVAMC IRB and Research and Development Committee on 3/13/2008, with necessary amendments to the protocol approved on 8/18/2008, 12/15/2008, 1/22/2009, 3/17/2009, 3/30/2009, 4/30/2009 and 5/26/2009.
- The DoD HRPO approved this protocol on 2/13/2009.

- Study personnel involved in the set-up and regulatory review process who were hired through the University of Pennsylvania subaward include statistical and neuropsychological consultants, IT support staff, and our research coordinator.

- **PROBLEMS ENCOUNTERED:**
  - Unanticipated sudden change in our investigative team: Personal issues regarding a family member, and requiring her full time attention, prompted Dr. Joan Cook, the co-principal investigator (Co-PI) of the award and primary investigator (PI) for the Connecticut site, to re-align her duties in November 2008. She relinquished her Co-PI status on the grant, to be replaced by Dr. Gerlinde Harb (formerly co-investigator) and Dr. Ilan Harpaz-Rotem. Dr. Harpaz-Rotem is a well-established Yale University/VACHS researcher, and he assumed Dr. Cook's duties as PI for the Connecticut site. This PI change needed to be approved by USAMRAA and CDMRP as well as by the three IRBs involved in the study (PVAMC, VACHS and Yale University), thereby delaying approval of the protocol by the HRPO and the hiring of personnel at both sites.
  - Technical and administrative delays at PVAMC:
    - To meet both the requirement of a VA-approved secure server and the technical requirements of the neuropsychological assessment computer program, this program had to be installed on a new server located in the PVAMC Mental Illness Research Education and Clinical Center (MIRECC). We therefore had to obtain IRB approval to host the program temporarily on an existing server on the VA network.
    - In January 2009, we encountered an unanticipated move of our research office to an adjacent building in the hospital, and subsequent administrative difficulties in setting up our new office (e.g. lack of phone and inter/intranet connections), delaying our ability to conduct any research by 5 weeks.
    - IT problem: We encountered a delay of several months in obtaining VA's permission to install the Firefox browser on our office desktop computer. This browser is essential for using the web-based computerized neuropsychological testing program.
    - IT problem: Although the IRB and HRPO had approved the use of digital video recording for this project, the PVAMC required a lengthy process of obtaining approvals from additional offices, the facility ISO and the facility IT department, in order to activate the USB port of our desktop so that the digital camera could be connected. Until final permission to install the camera software is obtained from IT, we must use the more cumbersome VHS technology to record treatment sessions. The lengthy procedure for obtaining permission to equip our office desktop with DVD-writing capacity was not yet completed by June 30, 2009; this capacity is essential for saving our recorded data.
    - Our staff has worked on developing a secure bi-site data entry system. This process was started in January 2009. Up until now there has not

been sufficient IT support at the PVAMC to complete it. Therefore, paper records that are accumulating as subjects are now being recruited and studied will need to be entered into a computer data base, en masse, at a later time.

B. VACHS, West Haven/Yale University:

- Regulatory review of the initial protocol was completed by the VACHS IRB and Research and Development Committee on 6/5/2008 and by the Yale University IRB on 11/12/2008. One amendment to the protocol was approved on 1/14/2009.
- The DoD HRPO approved this protocol on 2/24/2009.

- **PROBLEMS ENCOUNTERED:**
  - Because the Yale University IRB could review the protocol, including the one amendment, only after it had been approved by the VACHS IRB, the VACHS team was delayed in hiring staff necessary for the project. Therefore, the Connecticut site will begin recruitment at a later date than the Philadelphia site.
  - The change in the investigative team at the VACHS (see above) further delayed the start-up at this site.
  - Technical issues associated with VACHS staff accessing systems at PVAMC also have delayed the VACHS start date. After two months, during which time the PVAMC OI & T Service was tasked with granting VACHS access to the research server, we finally have been assured that a procedure is in place. Because PVAMC and VACHS are both VA sites, there had been no reason to anticipate that obtaining shared access to computer programs and data bases would raise any data security issues.
  - Dr. Harpaz-Rotem has identified a research team. However, he has needed to delay hiring of all the personnel until September 2009, by which time we expect that the computer access problems identified above will have been resolved. For budgetary reasons, it is important not to hire personnel too long before they can use computer systems necessary for carrying out the work of the project.

2. Recruitment, assessment and randomization of 80 participants at the PVAMC site and 80 at the VACHS site (total N=160).

A. Philadelphia VAMC:

- The PVAMC site began recruitment in April 2009, and has received 25 referrals from treatment providers in the Mental Health Clinic. All veterans referred to date have been male, with an average age of 36.2. Thirty-six percent (9) are African-American, 12% (3) Hispanic, 48% (12) Caucasian veterans, and 4% (1) Other ethnic background.
- Assessments were scheduled with 12 potential participants: five have completed the first assessment, and three veterans have completed the second assessment

as well. Three participants have been enrolled in the treatment study to date: two were randomized to IR + PPCI and one to PPCI alone.

- **PROBLEMS ENCOUNTERED:**
  - Additional technical problems: The secure PVAMC server hosting the neuropsychological test battery and database was abruptly, and without notice, shut down by facility IT personnel shortly after the start of recruitment in April 2009. Due to the shut-down and subsequent difficulties in rebuilding the server, we needed to suspend enrollment, causing a delay of 4 weeks.

B. VACHS, West Haven:

- As explained above, no recruitment has taken place at the VACHS site to date.
- Eight regular bi-site conference calls have served to help the VACHS site complete its set-up, assuring comparability of all study procedures at the two sites (December 2, 2008, January 29, 2009, February 12, 2009, March 12, 2009, April 7, 2009, April 28, 2009, May 12, 2009, and June 17, 2009).

3. Administration of six sessions of the protocol treatments to participants.

A. Philadelphia VAMC:

- The three enrolled veterans are currently participating in treatment, with one veteran having completed 5 sessions and another 3 sessions, and one scheduled for the first session.
- During Year One of this award, a detailed supervision plan as well as fidelity rating procedures were developed and implementation has begun.

B. VACHS, West Haven:

- As explained above, no treatment has taken place at the VACHS site to date.

4. Follow-up: re-assessment for detection of treatment effects and maintenance of benefits at 1 month, 3 months and 6 months post-treatment.

A. Philadelphia VAMC:

- Because recruitment was only recently started, no participants are in the follow-up phase of the study at this time.

B. VACHS, West Haven:

- No participants are in the follow-up phase at VACHS at this time.

5. Statistical analysis of the data and manuscript preparation.

- The project is in the data collection phase, and no statistical analyses currently are being done.

Section III: Key Research Accomplishments:

- Completion of lengthy regulatory reviews at 4 institutions

- Recruitment and hiring of staff at two sites
- Philadelphia site has initiated recruitment and enrollment
- West Haven site will initiate recruitment very soon

Section IV: Reportable Outcomes: Presentations:

The design of this research project was presented and well received at recent national and local conferences, for example the November 2008 annual meeting of the International Society of Traumatic Stress Studies (ISTSS), the National Mental Health Conference of the Department of Veterans' Affairs Employee Education System (July 2008), the CNS Injury Conference seminar series in the Department of Neurosurgery, University of Pennsylvania (April 2008), and the June 2009 annual meeting of the Associated Professional Sleep Societies (APSS). The project PI, Dr. Ross, will be presenting the project design at the upcoming meeting of the MHRF (Kansas City, MO; August 31 through September 3, 2009).

Section V: Conclusions:

Despite many major and minor delays, this research program is operational and recruiting at the PVAMC site. It is almost ready to initiate recruitment at the VACHS site. The lengthy Human Subjects regulatory review by four institutions was completed successfully during Year One. Recruitment is proceeding as planned at the PVAMC site; we have enrolled 3 participants in the treatment phase of the study during the initial 1.5 months of active recruitment. Continuing at this rate, we can expect to enroll 24 participants per year at the PVAMC site. Many of the problems that we have encountered were outside the purview of the research staff, and their resolution has depended upon the support of other institutional departments. Any remaining problems, specifically the finalization of a procedure for obtaining shared access by PVAMC and VACHS to programs and databases on a PVAMC research server, are nearing resolution; in the meantime, the latter issue is not interfering with recruitment at the PVAMC. We are confident that we now are in a position to focus on the recruitment and retention of participants in Year Two of this award.